REMARKS

Claims 41-52 have been canceled. New claims 53-60 have been added to more distinctly claim that which Applicants consider to be their invention and to advance prosecution. No new matter has been added and new claims 53-60 are supported by the specification.

1. Priority Date

It is stated that provisional applications 60/132,748 and 60/157,384 do not provide an adequate description of an antibody to the specific epitope of a prekallikrein-H-kininogen complex nor a human antibody.

In response, Applicants note that claims 46 and 47 have been canceled. In Applicants view, there is support for the subject matter recited in new claims 53-60, a method for preventing or treating a disorder using an antibody generated against HBP which binds to an epitope of heparin-binding protein which interacts with kininogen, in an amount effective to decrease release of bradykinin and in an amount effective to attenuate said alterations in endothelial cell permeability in said mammal. As noted in the response to the previous Office Action, both provisional applications do describe the generation of both monoclonal and polyclonal antibodies to HBP (see page 19, lines 25-30 for polyclonal antibodies and page 20, lines 1-9 for monoclonal antibodies in application serial no. 60/132,748 and analogously, page 17, line 23 to page 18, line 3 in application serial no. 60/157,384 for monoclonal and polyclonal antibodies). General descriptions are also provided on page 7, lines 8-17 in application serial no. 60/132,748 and on page 6, lines 27-32 in application serial no. 60/157,384. Applicants further point out that the effect of anti-HBP antibodies on endothelial cell permeability and evidence of HBP interaction with kininogen is shown in Example 2 of both provisional applications (see, for example, page 24, lines 17-28 which contains the section "Inhibition of HBP-induced increase in EC permeability by peptide HKH20-treatment"). This example shows the relationship of HBP binding to kininogen on

EC permeability. The antibodies generated prevented HBP-induced increase in EC permeability. Clearly, one of ordinary skill in the art would deduce that given that the disclosed anti-HBP antibody prevented HBP-induced endothelial cell permeability and that a kininogen-binding peptide had a similar effect, that such antbodies would also interact with kininogen. Therefore, Applicants should be entitled to the priority dates of the two provisional applications.

2. The Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 43-44 and 46-52 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing o particularly poitn out and distinctly claim the subject matter which Applicants regard as their invention. It is asserted that newly added claims 43-44 and 46-52 still do not set forth any structural characteristic of the protein. In response and in order to advance prosecution, claims 43-52 have been canceled. New claim 53 recites that the HBP has at least about an 80% identity with the amino acid sequence set forth in SEQ ID NO:1. Applicants reserve the right to file subsequent continuation and/or divisional applications on the canceled subject matter.

Claims 48-51 are asserted to recite "the HBP antagonist". In response, Applicants note that claims 48-51 have been canceled and the new claims recite –the anti-heparin bindingprotein antibody--. None of the new claims recite "the HBP antagonist".

In view of new claims 53-60 and the above-arguments, Applicants assert that the rejection of claims 43-44 and 46-52 have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

3. The Rejections Under 35 U.S.C. §112, First Paragraph

Claim 47 has been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention. In the Examiner's view, although the disclosure appears to support a role for HBP in the release of bradykinin from H-kininogen after cleavage by kallikrein, the disclosure does not appear to enable the actual binding of an epitope of HBP to the prekallikrein-H-kininogen complex, it does not appear to enable a monoclonal antibody to the proposed epitope of HBP. The Examiner in the Office Action acknowledges that an antagonist antibody that binds HBP does appear to inhibit the effects of bradykinin but asserts that it has not been established whether or not this effect involves the direct interaction of HBP and kininogen. Furthermore, the Examiner invites Applicants to provide objective evidence that HBP and kininogen directly interact to obviate the rejection.

First, Applicants note that claim 47 has been canceled. New claim 53 does incorporate the elements of prior claim 47. Furthermore in response to the points raised in the rejection, Applicants will submit as a Supplemental Response a Declaration under 37 C.FR. 1.132 by Thomas Renne, a collaborator of one of the inventors, Hans Flodgaard of the above-referenced application. In his Declaration, Dr. Renne will present results from experiments that show that HBP displaces H-kininogen assembled on the surface of immobilized Heparan sulfate or endothelial cells better than histidine-rich glycoprotein, factor XII or HK itself. These results certainly demonstrate that HBP and kininogen do directly interact.

In view of the above arguments, Applicants assert that the rejection under 35 U.S.C. §112, first paragraph has been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

4. The Rejections Under 35 U.S.C. §102

Claims 43-44 and 45 have been rejected under 35 U.S.C. §102(e) as anticipated by Oppenhelm et al. as evidenced by Rasmussen et al. Applicants traverse the rejection. However, in order to advance prosecution, Applicants have canceled claims 43-44 and 45.

However, Applicants reserve the right to file subsequent continuation or divisional applications directed to the canceled subject matter.

In view of the cancellation of claims 43-44 and 45, Applicants respectfully request that the rejections be withdrawn.

5. The Rejections Under 35 U.S.C. §103

Claims 43-46 and 48-52 have been rejected under 35 U.S.C. §103 as being unpatentable over Oppenhelm et al. as evidenced by Rasmussen et al. in view of Grunfield et al. Applicants traverse the rejection. However, in order to advance prosecution, Applicants have canceled claims 43-46 and 48-52. However, Applicants reserve the right to file subsequent continuation or divisional applications directed to the canceled subject matter.

In view of the cancellation of claims 43-46 and 48-52, Applicants respectfully request that the rejections be withdrawn.

6. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone at (914) 712-0093 if there are any questions concerning this amendment or application.

Respectfully submitted,

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